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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,307	01/11/2001	Sam J. Milstein	1946/1A483-US8	8759

7590 10/06/2005

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EXAMINER	
YEBASSA, DESTA LETTA	
ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 10/06/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/760,307	MILSTEIN ET AL.	
	Examiner	Art Unit	
	Desta L. Yebassa	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *03 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13-37,50-73,87-110 and 112-189* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13-37,50-73,87-110 and 112-189* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *Jul 27 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

SDD

DETAILED ACTION

Receipt is acknowledged of applicant's remarks and amendment filed on 06/03/05.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 13-36, 50-73, 87-110, and 112-189 arc rejected under 35 U.S.C. 103(a) as being unpatentable over Makino et al (US Patent No. 4,746,675) in view of Morishita et al (US Patent No. 4,873,087).

Makino et al. teaches external pharmaceutical composition for administering therapeutic agents via skin and mucosal membranes. The compositions of Makino comprise a pharmacologically active agent and a penetration enhancer, such as pyroglutamic acid derivatives (col. 4-8). The pyroglutamic acid derivatives shown by

formula I (col. 4) of Makino read on the claimed acylated amino acid derivatives. Makino teaches a number of pharmaceutically active agents that can be administered using the above absorption enhancer (col. 10-12), which include those that are claimed in the instant application. Makino teaches that the penetration enhancers are capable of penetrating skin or mucosa and thus can enhance the absorption a wide range of (hydrophilic as well as hydrophobic) drugs; and also when administered by oral or injection route, the absorption enhancer prevents the drug from being degraded and maintain the effective blood levels over a long period of time (col. 3-4).

Morishita teaches a preparation containing an absorption promoter and a medically active agent for promoting absorption through a gastrointestinal organ such as colon, rectum or through vagina. The absorption promoter substance of Morishita is an N-acyl amino acid or N-acyl peptide derivative, of formula I (col. 1, lines 5-15, col. 3, lines 13-15) and is obtained by the reaction of an acid (R-COOH) with an amino acid or peptide. The carboxylic acids and amino acids used for preparing N-acyl amino acids are described in col. 4 and 6 and include those described in the instant specification. Among the medically active agent, Morishita describes hormones, such as insulin, antibiotics etc (col. 5, lines 25-68. Morishita does not specifically teach subcutaneous, intranasal or sublingual delivery routes, instead teaches administration through rectum or vagina, which are lined by mucosal membranes.

Response to Arguments

1. *Obviousness-type double patenting rejection*

In response to the obviousness-type double patenting rejection, applicants agreed to file a terminal disclaimer, upon finding allowable subject matter. However, no such has been filed. Accordingly, the obviousness-type double patenting rejection of record has been maintained.

2. *Common ownership rejection*

In responses to the common ownership rejection, applicants agreed to submit a declaration under 103(c), upon finding allowable subject matter. However, no such has been filed. Accordingly, the common ownership rejection of record has been maintained.

3. Rejection under 35 U.S.C 103(a)

Applicant argue there is no evidence in the cited references that the absorption promoters in Morishita, or the penetration enhancers of Makino necessarily provide a biologically active agent in an intermediate conformational state, Morishita and Makino do not explicitly disclose transforming or providing a biologically active agent in an intermediate conformational state. Furthermore, applicant argues Morishita does not disclose subcutaneous administration.

Applicant's arguments filed 06/03/05 have been fully considered. However, applicants' arguments are not persuasive because applicants did not argue the fact that the cited references disclose or suggest the components of the claimed composition. While the references teach rectal compositions, instant claims do not specifically distinguish the claimed composition from that of the prior art compositions so as render the compositions of prior art unsuitable for the claimed routes of delivery. Absent any

feature that limits the compositions specific to the claimed delivery routes, the invention has no patentable weight and the compositions of Morishita and Makino are suitable for administration via the claimed routes.

The claimed routes of sublingual, intranasal involve mucosal administration. Therefore, it would have been obvious for one of an ordinary skill in the art at the time of the instant invention to employ the pyroglutamic acid derivatives of Makino as absorption enhancers for a variety of pharmaceutical agents, administered by sublingual or intranasal or subcutaneous routes because Makino teaches that the compounds are extremely useful in delivering drugs orally, topically or mucosally without loosing the activity due to degradation or lack of transport through the mucosal or epidermal membranes (column 3-4 and column 10-12). Similarly, it would have obvious for one of an ordinary skill in the art at the time of the instant invention to administer the absorption enhancers of Morishita via mucosal routes (sublingual or intranasal) or subcutaneous injection because Makino suggests that the amino acid derivatives are effective in delivering a number of drugs administered by oral or injection or via skin or mucosal membrane, without loosing the activity of the drugs. Therefore, for the reasons stated above, applicant's argument are found unpersuasive and the prior art rejections are maintained.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Telephonic Inquiry

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Desta Yebassa whose telephone number is (571) 272-8511. The examiner can normally be reached Mon.-Friday 8:00 - 6:00.
If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Thurman K. Page can be reached on (571) 272-0602. The fax phone Number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application information Retrieval (PAIR) system. Status information for

Published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

You have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

Desta L. Yebassa
Patent Examiner
Art Unit 1615

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